REMARKS

Applicant thanks Examiner for clarifying, in a telephone interview of September 25, 2007, that claim 10 is allowable.

Response to Claim Rejections Under 35 U.S.C. § 103

Examiner has rejected claims 1-6, 8-9, 23-25, 27-31, 33-36, 38, 40, 42, and 45 as being obvious over either Rosenfield or Zouboulis in view of Bryan. Applicant thanks Examiner for recognizing that the Declaration of Applicant Zouboulis demonstrates that the cells of this invention are novel and nonobvious. Applicant has amended claim 1 to specifically state two characteristics of normal, non-transfected and differentiating sebocytes that are present in the claimed immortalized sebocytes, that is, production of lipids, and response to androgens and/or retinoids. Applicant has, in addition, canceled claims 8, 27, 33, 38, 42, and 45.

With respect to amended claim 1, none of the references cited by the Examiner, Zouboulis, Rosenfield, or Bryan, individually or in combination teach the use of a technique for immortalization of sebocyte cell culture to produce an immortalized sebocyte cell line having the characteristics of production of lipids or proliferation response to androgen and/or retinoids. As Applicant has previously noted, Rosenfield is directed to the cultivation of cells from the preputial gland derived from a transgenic mouse homozygous for a temperature sensitive strain of SV40 T, while Zouboulis is directed to the use of non-immortalized sebocyte cultures for the study of seborrhea and acne. Bryan is generally directed to the immortalization of human cells using SV40 T.

Further, under *KSR v. Teleflex* and the recently published guidelines, Examiner should base an obviousness rejection of the claimed cells only if a factual showing can be made that the claimed cells involve "Applying a known technique to a known device (method, or product) ready for improvement to yield *predictable* results." Applicant further notes that Bryan actually teaches away from the proposition that SV-40 immortalization could predictably be used to produce immortalized cells, such as sebocytes, having the differentiated characteristics of the non-immortalized cells. Bryan states that while some SV-40-immortalized cells retained the differentiated characteristics of the non-immortalized cell, "some SV-40 established cell lines may lose

many of their differentiated properties and take on a more transformed phenotype." Bryan at 339. Bryan notes that immortalized keratinocytes (a type of skin cell) have lost differentiated functions at temperatures permitting growth. Thus, Examiner has not made a *prima facie* case that the methods of SV 40 immortalization could be used on known sebocyte cultures to predictably produce an immortalized sebocyte with differentiated properties (such as lipid expression or response to androgens).

Applicant, in his declaration of August 18, 2006, has shown that it was far from obvious at the time of the invention to obtain an immortalized sebocyte having the characteristics of amended claim 1, as demonstrated by the long felt need for such a sebocyte, the past and continued failure of others. Applicant has noted the failure of others by noting that others had attempted to produce a line of immortalized sebocytes, but had failed to do so by the date of this invention. Further, the Applicant has stated that his own efforts to employ known methods of immortalizing cells, methods which had been successfully employed on cells similar to sebocytes, failed to produce an immortalized sebocyte cell line having the characteristics of amended claim 1. It was only with Applicant's own research findings that mature facial skin cells may yield immortalized sebocytes that preserve major characteristics of normal sebocyte behaviour and produce lipids, and Applicant's intensive screening of many samples of skin cells taken from many human body sites and subjects, that the Applicant was finally able to obtain an immortalized cell line having the characteristics of amended claim 1. Applicant has thus shown that producing an immortalized sebocyte with the characteristics of claim 1 from any human source was not obvious at the time of invention. Applicant has further provided evidence of commercial success of the invention, by showing that the immortalized sebocyte lines have been successfully licensed to fourteen pharmaceutical and cosmetic companies, eight of which have annual sales in excess of $2 billion, nine of which have annual sales in excess of $500 million, and 11 of which have annual sales in excess of $100 million. As further evidence of commercial interest in these immortalized sebocytes, there have been 29 original manuscripts reporting on research utilizing the immortalized sebocytes. Lastly, the continued failure of others is evidenced by the fact that only one other investigator, Dr.

Thiboutot, has been able to produce an immortalized sebocyte cell line having sebocyte characteristics, and only by exactly following the procedures first outlined by Applicant.

Claims 2-6, 9, 23-25, 28-31, 34-36, and 40, being dependent from claim 1, are nonobvious over the cited references for the same reasons as claim 1 and on their own merits. In particular, with respect to claims 6, 25, 31, 36 and 40, the Declaration of Dr. Zouboulis demonstrates the failure of others, and Applicant's own extensive efforts to produce a sebocyte that expresses a SV-40 large T antigen (indicating that it has been immortalized by SV-40), as well as having the normal sebocyte function of expressing lipids.

Examiner has rejected claims 63-65 as being obvious over either Rosenfield or Zouboulis in view of Bryan. Applicant has amended claim 63 to include the limitation that the proliferation of the sebocytes is modifiable by an androgen and/or a retinoid.

With respect to amended claim 63, Applicant has incorporated the limitations of newly added claim 70. As stated previously, none of the references cited by the Examiner, Zouboulis, Rosenfield, or Bryan, individually or in combination, teach the use of a technique for immortalization of sebocyte cell culture to produce an immortalized sebocyte cell line having differentiated properties, such as producing the listed antigens or that is modifiable by an androgen and/or retinoid. Furthermore, as stated in the August 18, 2006 declaration of Applicant Dr. Zouboulis, it was not obvious at the time of the invention to apply known immortalization techniques to sebocytes to obtain immortalized sebocytes having the characteristic that it is modifiable by an androgen and/or retinoid. In particular, Applicant's declaration demonstrates the failure of other researchers to produce an immortalized sebocyte, and by Applicant's own difficulty in obtaining a sebocyte having the characteristics of responsiveness to androgens or retinoids.

Claims 64 and 65, being dependent from claim 63, are nonobvious over the cited references for the same reasons as claim 63 and on their own merits. Claims 71 and 72, being dependent from claim 70, are nonobvious over the cited references for the same reasons as claim 70 and on their own merits.

Examiner has rejected claims 66-68 as being obvious over either Rosenfield or Zouboulis in view of Bryan. Applicant has amended claim 66 to include a limitation that the immortalized sebocyte cell is derived from a human.

With respect to amended claim 66, none of the references cited by the Examiner, Zouboulis, Rosenfield, or Bryan, individually or in combination, teach the use of a technique for immortalization of sebocyte cell culture to produce an immortalized sebocyte cell line having the characteristics of production of lipids, and as stated previously, the Bryan reference teaches away from the idea that SV-40 immortalization can be employed to predictably produce an immortalized cell with differentiated characteristics. Furthermore, as stated in the August 18, 2006 declaration of Applicant Dr. Zouboulis, it was not obvious at the time of the invention to apply the known techniques to produce an immortalized sebocyte having the property of expressing lipids. This is demonstrated by the failure of other organizations to obtain immortalized sebocytes, and Applicant's own difficulty in applying techniques known for immortalizing other skin cells to sebocyte cultures. It was only after an extensive screening of samples of cells from various body sites and human subjects, along with Applicant's experimental insight that mature facial skin cells may yield immortalized sebocytes that preserve major characteristics of normal sebocyte behavior and produce lipids, was applicant able to produce sebocyte cells having the feature of lipid expression. As discussed above, further evidence of the commercial success of the discovery of the immortalized sebocytes is demonstrated by the extensive licensing of the cells and extensive published research using these cells, as well as the continued failure of others to produce immortalized sebocytes other than by the methods of Applicant.

Claims 67 and 68, being dependent from claim 66, are nonobvious over the cited references for the same reasons as claim 66 and on their own merits. Especially with respect to claim 69, the Declaration of Dr. Zouboulis demonstrates the failure of others, and Applicant's own extensive efforts to produce a sebocyte that expresses a SV-40 large T antigen (indicating that it has been immortalized by SV-40), as well as having the normal sebocyte function of expressing lipids.

CONCLUSION

All claims presently in the application are believed to be allowable over the art of record and early notice to that effect is respectfully solicited. Applicant requests a one month extension to respond and also files a Request for Continued Examination, and authorizes a charge of $930 for the extension and request to Deposit Account No. 19-4972. Applicant requests that any further fees for extensions or for additional claims be charged to Deposit Account No. 19-4972.

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Respectfully submitted,

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